Research Paper

Volume : 3 | Issue : 6 | June 2014 • ISSN No 2277 - 8179

Structurally Significant Analysis of Tuberculosis Proteins

Biotechnology

KEYWORDS : Tuberculosis (TB), protein Data Bank (PDB), CaPTURE (Cation-pi Trends Using Realistic Electrostatics), energetically significant.

Syeda Shaizadi Meraj. Dept. Of Biotechnology, The Oxford College Of Engineering (Toce), Bommanahalli, Hosur Road, Bangalore 560068

Tanusree Chaudhuri. Dept. Of Biotechnology, The Oxford College Of Engineering (Toce), Bommanahalli, Hosur Road, Bangalore 560068

ABSTRACT

In this paper the main focus is on the energetically significant cation-π interaction of the structurally well resolved TB proteins. TB is a disease caused by a bacterium called Mycobacterium tuberculosis. The bacteria usually attack the lungs, but TB bacteria can attack any part of the body such as the kidney, spine, and brain. If not treated properly, TB disease can be fatal. Cation-π interaction plays an important role in protein structure, molecular recognition and enzyme catalysis. The residues which are involved in the cation-π interaction are Lysine, Arginine and the aromatic side chains of Phenylalanine, Tyrosine, and Tryptophan. We have analyzed cation-π interaction on a data set of 12 TB proteins where the structural resolution of the protein was 3 Å and more. It was observed that there was more number of energetically significant pairs present between Arg/Tyr compared to other pairs. Using CaPTURE program we have determined totally 57 energetically significant pairs in a data set of 12 TB proteins

1. INTRODUCTION

Tuberculosis (TB) remains a major global health problem. It causes ill-health among millions of people each year and ranks as the second leading cause of death from an infectious disease worldwide, after the human immunodeficiency virus (HIV). The latest estimated reports according to World Health Organization (WHO) are that there were 8.6 million new TB cases in 2012 and 1.3 million TB deaths (just under 1.0 million among HIV-negative people and 0.3 million HIV-associated TB deaths) [1]. Cation-π interactions are non covalent binding forces that occur between cations and π systems. Cationic moieties such as Arginine (R) and Lysine (K) that are within 6.0 Å of the face of an aromatic ring such as phenylalanine (F), tyrosine(Y), & tryptophan (W) may engage in polar interactions called cation-π interactions [2]. Over one fourth of Trp's in the Protein Data Bank interact with cations, and 99% of significant cation-π interactions occur within a distance of 6.0 Å [2]. Cation-π interactions are usually energetically important when the ligand has either positive charge or an aromatic ring [3].Therefore in this paper we have identified 12 PDB structures with x-ray resolution greater 3 Å and more [4].

2. MATERIALS AND METHODS.

2.1 Searching of Protein Data Bank

The tuberculosis (TB) proteins were taken from essential gene list present in Mycobacterium tuberculosis Structural Database (MtbSD) [5].From the essential gene list first PDB ids were taken among several ids corresponding to unique Rv ids, which were around 313 PDB ids in total. Ultimately a set of 12 PDB IDs was obtained with the following advanced search criteria of protein data bank [4].

(i) All the redundancies were removed from the 313 PDB IDs,
(ii) The X-Ray Resolution of the proteins was solved at 3.0 and more Å [2, 4] as structurally well resolved proteins provides a better accuracy to our result

The PDB IDs of the proteins taken for further study are: 1G18, 1HX5, 1MRU, 1SJP, 1ZAU, 2A87, 2G88, 2OAR, 2QJ3, 2WTZ, 2ZHX, and 3FOQ.

These Pdb ids indicate the proteins whose structures are well resolved by the X-Ray crystallographic method.

2.2 CaPTURE

The CaPTURE program can identify energetically significant cation-pi interactions within proteins in the Protein Data Bank (PDB) [2]. Cation-π interactions in 12 tuberculosis proteins were determined by using CaPTURE (Cation-pi Trends Using Realistic Electrostatics) computational program developed by Gallivan and Dougherty at Cal Tech [6].

3. RESULTS

3.1 Energetically significant cation-π

The 12 TB proteins were analyzed for energetically significant cation-π interactions. It was found that 57 energetically significant cation-π interactions were determined in combined 12 PDB ids. The pair wise significant cation-π interaction energy between the positive amino acid residue i.e Arg/Lys and aromatic residues i.e Phe, Tyr & Trp shows that Arg residue forms a more number of significant pair with the three aromatic resides than Lys, where there is no significant pairs forming between Lys/Phe & Lys/Trp and only single significant pair forming between Lys/Trp which is comparatively less when compared with aromatic residues forming pairs with Arg residue as shown in Figure 1. Arg/Tyr (-111.98) energy is strongest; Lys/Phe & Lys/Trp does not show any energetically significant interactions. Lys/Tyr (-17.69) is lowest among the possible pairs. Each individual energetically significant Cation-π residue pair is shown in the Table 1.

4. DISCUSSION

We have analyzed the influence of the cation-π interaction on the TB proteins. Among the 57 energetically significant interactions, Arg/Tyr pair shows a highest energetically significant interaction (-111.98), i.e the total of both electrostatic E (es) and van der waals E (vdw) interactions. The CaPTURE program computes both the electrostatic E (es) and van der waals E (vdw) energies of interactions with the calculated total interaction energy being defined as the sum of these two. The energetically important cation-π interaction were defined as those interactions whose total interaction energy is more negative than -2.0 Kcal/mole (2),(6). The effectiveness of the cation-π interaction is found in different neurological disorders, including Parkinson's disease, Alzheimer's disease, schizophrenia, depression and autism [7]. Hence it is possible that cation-π interactions play a very significant role in structural stability of the TB.

5. ACKNOWLEDGEMENT

We would like to thank Department of Bio-technology, The Oxford College of Engineering, Dr. Jaleel UCA, Principal investigator CSIR, OSDD and Syed Mohammed Aminuddin Aftab PhD-Scholar Department of Aerospace Engineering Universiti Putra Malaysia for their help and support.

Figures

Figure 1: Fig showing Cation-π pairs involved in energetically significant interaction.

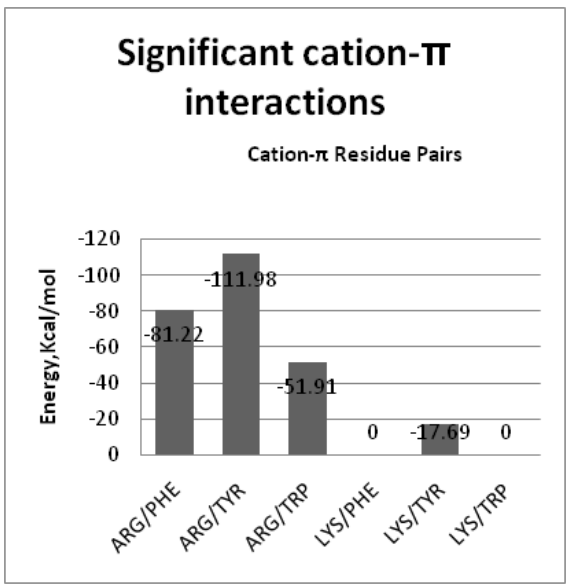

TABLE 1: Table showing energetically significant pair present among the 12 TB PDB s.

PDB CODE	ARG/PHE	ARG/ TYR	ARG/ TRP	LYS/ PHE	LYS/ TYR	LYS/ TRP	No of Energetically Significant interactions
1MRU		-1.33 -4.07 -1.36 -3.97 -6.21 -3.3 -2.46 -3.33 -2.67 2.75			-3.62 -0.42		6
1SJP					-4.71 -2.43 -3.16 -1.52 -1.01 -0.82		3
2A87	-2.58 -1.02 -1.86 -2.31 -1.3 -1.77 -2.64 -3.46 -1.8 -2.44 -2.28 -1.02 -2.6 -1.24 -1.01 -2.81 -1.28 -1.93	-1.57 -1.25 -1.92 -3.04					11
2QJ3	-1.73 -1.68 -1.7 -1.29						2
2WTZ	-1.19 -1.19 -1.16 -1.54 -1.46 -1.41	-1.41 -1.56 -2.57 -2.52	-4.04 -3.41 -2.24 -3.24				7
2ZHX	-2.83 -2.83 -2.87 -3.13 -2.84 -2.92 -2.51 -1.14 -1.21 -1.21 -1.28 -1.26 -1.17 -1.23	-4.09 -2.54 -3.69 -2.49 -3.91 -2.53 -3.22 -2.86 -2.34 -4.4 -2.39 -3.92 -2.79 -2.61 -2.43 -0.85 -2.83 -0.98 -2.84 -3.18 -3.21 -2.7 -1.04 -2.71 -1.27 -2.37	-3.65 -4.27 -4.03 -4.16 -3.85 -1.13 -2.32 -1.38 -1.85 -0.96 -1.63 -1.23				27
3FOQ	-1.93 -1.16						1
Total	-81.22	-111.98	-51.91	0	-17.69	0	57

Volume : 3 | Issue : 6 | June 2014 • ISSN No 2277 - 8179

REFERENCE

[1]Organization WH, others. Global tuberculosis report 2013. World Health Organization; 2013. | [2]Gallivan JP, Dougherty DA. Cation-pi interactions in structural biology. Proceedings of the National Academy of Sciences. 1999;96(17):9459–64. | [3]Zacharias N DD. Cation-pi interactions in ligand recognition and catalysis. Trends Pharmacol Sci. 2002;23(6):281–7. | [4]Berman H, Henrick K, Nakamura H, Markley JL. The worldwide Protein Data Bank (wwPDB): ensuring a single, uniform archive of PDB data. Nucleic acids research. 2007;35(suppl 1):D301–D303. | [5]Hassan S, Logambiga P, Raman AM, Subazini TK, Kumaraswami V, Hanna LE. MtbSD-a comprehensive structural database for Mycobacterium tuberculosis. Tuberculosis (Edinb). 2011;91(6):556–62. | [6]Staiger J. An Analysis of Cation-pi Interactions in Cytochrome F. ProQuest; 2007. | [7]Zhong W, Gallivan JP, Zhang Y, Li L, Lester HA, Dougherty DA. From ab initio quantum mechanics to molecular neurobiology: a cation-pi binding site in the nicotinic receptor. Proceedings of the National Academy of Sciences. 1998;95(21):12088–93. |